eclampsia be accurately foreseen and avoided by the careful attendant upon the case; and does albuminuria, or even a renal sediment, predict with any degree of accuracy parturient or puerperal eclampsia? By way of answer the following conclusions seem warranted at the present time:

1. Careful urinalyses should be carried out in all cases of pregnancy at frequent intervals, and with increased frequency as term is approached.
2. The most dependable indications of impaired renal function and of probable eclampsia have been shown by general experience to be the presence of decided quantities of serum albumin, the diminution of the eliminated urea, and the presence of a microscopic renal sediment (casts, renal epithelium, blood, etc.). The character of the latter, when accompanied by the well-known clinical signs of nephritis, always constitutes a working basis for an estimate of the probability of imminent danger.
3. Even if the urine appear perfectly normal the possibility of eclampsia must be considered, especially in young women. Eclampsia in such cases is of equal severity with that of cases in which the urine has given due warning of impaired renal functions.
4. When eclampsia supervenes upon labor in a subject with previously (apparently) healthy kidneys, the tendency subsequently is toward a return to normal renal functions if the patient survives. This circumstance would seem to indicate still more strongly that the kidneys may actually have been normal up to the time of a temporary embarrassment and suspension of function.
5. Until the nature and ultimate cause of uræmia and eclampsia are more thoroughly understood, it would appear that urinalysis, though not an unerring guide, is our most valuable index of the condition of the kidneys and our most trustworthy source of information as to danger from such forms of toxæmia.
6. The prognosis seems to be vastly improved if eclampsia be combated by generous bleeding, followed by venous transfusion with normal salt solution. These measures reduce and dilute the poison in the circulation, and relieve the cardiac distress. Free diaphoresis and purging are of course indicated.

A NEW METHOD OF GASTRIC PROTEOLYSIS.[1]

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The essential chemical function of the stomach is the digestion of proteids. While digestion of fats has recently been shown to take place in the stomach, as well as in the intestine, it is always insignificant quantitatively. Digestion of (cooked) starches occurs within but not by the stomach, and may be very considerable, although no complete systematic study of this phase of digestion has been made as yet, and it is obvious that this phase of gastric digestion must be extremely variable. The method of gastric analysis submitted by the writer in 1900 to the Prize Committee of the American Medical Association, and published in the *Journal* of that body March 27-30, 1901, differed from the various clinical methods in vogue, in attempting to investigate directly the actual amount of digestive function performed, instead of measuring the acid, ferment or other potential energy remaining after the extraction of the stomach contents.

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[1] Presented in abstract to the American Gastroenterological Association, 1903.

On account of the small quantity of raw material available in practical gastric analysis, the necessity of performing many manœuvres upon the clear filtrate, which seldom exceeds 50 per cent. of the total quantity extracted, and the necessity of using separate portions of the filtrate for other methods of examination, as those for acidity, peptic strength, and qualitative composition, it became evident to the writer, very early in his preliminary study of the problem, that exact scientific analysis of proteids was out of the question, even if it could be adapted to the use of the clinician. For this reason it was decided to employ the general method of centrifugal precipitation, and to throw out of solution the various proteids in successive groups corresponding to the degree of peptonization, and employing as precipitants substances which should produce fairly bulky precipitates, which should not precipitate non-proteid ingredients of chyme, nor result in confusing mutual reactions. By consulting the qualitative tables of proteid precipitants collated by Ewald, Gamgee, and others, some idea may be formed of the very considerable amount of preliminary study required, as, for one or other of the reasons mentioned, most of the reagents suggested were found inapplicable to the problem propounded.

Anyone who has used the centrifuge to any extent in clinical estimations of any kind, will assent to the statement that the only safe rule is to base a volumetric reading on the minimum obtained after several successive centrifugalizations at a considerable speed. Whether the hand, water, or electric centrifuge is employed, the maximum speed obtainable for tubes of considerable size, without great risk of breaking the glass and spoiling the result, is 2000 to 2500 revolutions per minute. The writer has obtained identical results with the hand and water instruments, and has always centrifugalized until the precipitate suffered no further diminution in volume. Usually three centrifugalizations of two minutes or more each have been used.

As originally reported, three precipitates were compared, dealing in all instances with an investigandum of 10 c.c. of clear filtrate from chyme, and using graduated tubes, which enabled the readings to be made directly in percentages of this amount. These precipitates were, successively: soluble albumin,[1] precipitated by heat alone; syntonin and albumoses, precipitated by saturation with ammonium sulphate; peptones, purin bodies, amido-compounds, etc., precipitated by phosphomolybdic acid.

From an investigation of about twenty normal cases and over one hundred abnormal ones the following data have been obtained:

	Minimum.	Average or normal.	Maximum.	
Albumin . .	trace.	2–4 per ct.	7 per ct.	
Albumose . .	trace.	½–1 "	3 "	(faint cloud always remained in suspension.)
Peptone . .	5 per ct.	20–30 "	47 "	

With regard to the last line, it should be said that less than 15 per cent. is rarely found, except some hours after a meal, or unless evidence of low peptic and acid power is forthcoming. The maximum precipitate given includes albumoses, the highest precipitate found for peptone alone being 36 per cent., and, otherwise, the highest for peptone alone or albumose and peptone together—albumose never being sufficient to increase the precipitate materially—being 33 per cent.

The albumose precipitate being always scanty and inconclusive for practical purposes, I have for some time followed the suggestion of Dr. G. H. A. Clowes, and have simplified the procedure so as to precipitate soluble albumin by heat and then all further products by phosphomolybdic or phosphotungstic acid. On account of the sharp demarcation between these two precipitates, it is unnecessary to decant from the former, but the volume of the second precipitate may be read beginning at the top of the first. The weight of the second will, however, compress the first considerably, say from 2 per cent. to 1 per cent., or from 4 per cent. to 2 per cent. For comparative purposes, the first reading is taken without this compressive effect.

It is of interest to translate these readings by volume into percentages by weight. The volume of albumin represents about one-fifth as much by weight. The volume of "peptone" by phosphomolybdic or phosphotungstic acid represents about four times the bulk obtained by tannin, in those instances in which the absence of starch—which is also precipitated by tannin and which may be present when the qualitative test for erythrodextrin masks it—allows a comparison to be made. The tannin precipitate, in turn, represents about the same exaggeration of the percentage by weight as in the case of albumin. Thus, the volumetric percentage of peptone represents an exaggeration of the weight percentage by about 20. However, these statements are not intended in an accurate quantitative sense, but merely to afford a general idea of the magnification, so to speak, obtained from this method. Like other clinical methods, it is intended only for comparative use, and must not be interpreted in too literal a sense.

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[1] In the original report this was called *acid albumin* or *syntonin*. Although after the ordinary test meal all soluble albumin has become so through the action of acid, it is not *acid albumin* in the technical sense until it becomes uncoagulable by heat.

So far as I am able to learn, there are no conditions liable to be encountered in stomach contents, obtained in the usual way and examined with a fair degree of promptitude, which interfere with or notably diminish the precipitates mentioned. Obviously, if the albumin precipitate were allowed to stand for a long time in either an acid or alkaline medium, resolution would occur, but no notable diminution of bulk can occur during the test as ordinarily performed. Nor, on the other hand, is there any extraneous precipitate obtained by boiling the acid filtrate, which can add to the apparent bulk of albumin. It may be remarked here that the properly prepared filtrate is almost absolutely free from mucin.

The precipitate by phosphomolybdic or phosphotungstic acid certainly does not consist of pure peptone. It was formerly taught that gastric digestion ended with the formation of peptone, but we now know that amido-compounds—using the word in a rather loose chemical sense—are formed, as in pancreatic digestion. I have noticed that in comparing the "peptone" precipitate of the same filtrate, before and after standing at room temperature for a day or two, a considerable diminution in volume may occur, which is probably due to chemical change beyond the stage of peptones proper. If so, the volume of the "peptone" precipitate is probably not materially exaggerated by the progress of digestion beyond the nutritive stage.

The lower proteids having been already removed, the "peptone" precipitate of filtered chyme may theoretically include peptones proper, amido-derivatives of proteids, amido-acids of bile, ammonium salts, alkaloids, and purin bodies. Any considerable admixture of bile spoils the sample for any kind of systematic analysis. Moreover, bile acids would be precipitated by HCl and excluded from the investigandum, unless there existed an absence of free HCl. Ammonium salts do not interfere materially, for even a 10 per cent.—practically a saturated—solution of ammonium sulphate yields less than 1 per cent. volumetric precipitate with phosphomolybdic acid, and an amount of ammonium demonstrable by the ordinary rough tests is almost never found in chyme. Alkaloids are, of course, never present in any appreciable quantity. In my report in 1900 the statement was made that phosphomolybdic acid did not precipitate with normal urine, although a blue color was produced. This statement is incorrect, as a small (usually 1 per cent. to 4 per cent.) but perfectly distinct precipitate is produced. The experiment was repeated several times, so that the discrepancy cannot be ascribed to a single exceptional urine, and the observation is so simple that the personal equation need not be considered. Doubtless, there was some imperfection in the reagent obtained for the control experiments with urine.

I have noticed a peculiar reaction with starch. Phosphomolybdic acid does not precipitate with a solution of HCl corresponding to the ordinary maximum in gastric juice, nor with a concentrated solution of starch. When, however, phosphomolybdic acid is added to a concentrated solution of starch, also containing hydrochloric acid in gastric strength, a precipitate up to 4 per cent. by volume may be obtained. This reaction well illustrates a possible fallacy in dealing with complex mixtures of organic and inorganic substances, for, aside from mutual reactions to produce insoluble substances, which form an important part of inorganic analysis, a genuine precipitation may drag down other substances in a mechanical way, or various changes of conditions may influence the solubility of certain substances. It is obvious that the method of analysis described follows the plan of successive precipitation and removal which characterizes the "wet method" of inorganic analysis. It is equally obvious that organic substances do not interact with the same definiteness as inorganic and that the conclusions drawn cannot be so absolute. Nitrogen estimations have naturally suggested themselves as a means of gastric analysis, and have been employed in different ways by various chemists. Unfortunately, the estimation of nitrogen does not afford a clue to its source from this or that proteid or proteid-derivative, and the nitrogen percentage of albumin, albumose, and peptones in the generic sense is nearly the same, while, on the other hand, nearly or quite as great variations of nitrogen percentage may occur within each of these groups. It is theoretically possible to analyze quite accurately the various proteids of chyme. The process is, however, altogether too difficult for ordinary clinical use, and I am informed that it is impossible, even for an expert chemist, to make such an analysis with the small quantity of investigandum available —usually less than 20 c.c. of filtrate, after allowing for the ordinary acid titrations.

In order to determine how far the so-called peptone precipitate might be increased by the reaction with purin bodies, the following experiment was applied to a number of cases—about ten in all. The liquid above the strata of albumin by heat and remaining proteids, etc., by phosphomolybdic acid was decanted and the precipitates dissolved, so far as possible, by liquor potassæ. The remaining sediment was again centrifugalized and was found to amount to about 0.5 per cent. (taking the 10 c.c. as 100 per cent.) by volume of a beautiful, navy-blue pigment. I am informed by chemists that this is a reduction product of molybdenum, of unknown constitution. It is, however, probable that the potassium hydroxide redissolves other than the strictly proteid precipitates. Still, from the *a priori* probability that non-proteid precipitable substances are present in minute amount, from the experiments with urine and with starch and HCl, it seems a warrantable deduction that the so-called peptone precipitate is not exaggerated by more than 5 per cent. (taking 10 c.c. of original filtrate as 100 per cent.), and this possible fallacy does not interfere materially with the practical value of the test.

Realizing, then, that we are employing a purely clinical and approximate method of comparing the proteolytic power of different stomachs or of the same stomach at different times, the question presents itself, What practical conclusions can be drawn from the results? In looking over my tables, it has not been possible to recognize a definite relation between the proteid precipitates and any other single object of the routine examination, such as acidity. This is by no means a condemnation of the method. If proteolysis were a mathematical function of some other measurable factor, it would not be necessary to attempt the former investigation at all.

A priori, it would seem that the albumose precipitate or this and the peptone precipitate should rise and fall with the amount of combined hydrochloric acid, but I cannot discover any such direct relationship. However, in a series of notes on gastric analysis, published in *American Medicine* in 1902–1903, I have shown the fallacies of the sodium-tungstate test for combined acidity, and that by alizarin is probably not much better. Incineration methods are not adapted to clinical study, but it is possible that a really accurate estimation of combined hydrochloric acid would show a correspondence to the proteolytic tests.

When the albumin precipitate is high and the peptone precipitate low, poor digestion is suggested. One of the reasons for abandoning the separate precipitation of albumose was that the intermediate position of this precipitate and its small amount prevented any positive deduction. It often happens, however, that there is an abundant precipitate in both or all three steps in the process. This suggests that there has been a recent acceleration in the acidifying or early stages of digestion, and certainly does not seem to indicate an impairment of digestion. On the whole, the most definite information seems to depend upon the amount of the final precipitate, which should amount to 20 per cent. to 30 per cent. Generally speaking, there is a fair correspondence between what has been alluded to as the optimum precipitates and a fairly normal acidity and ferment test. For instance, we may compare two tests made on the same case under similar conditions:

Total acidity.	Free HCl.	Combined HCl.	Albumin.	Albumose and peptone.	Rennet test.
48	22	19	trace.	8 per ct.	Weak.
90	45	29	1 per ct.	26 "	Strong.

When the investigandum is obtained late after a meal the digested proteids are low, usually about 10 per cent., whether the hydrochloric acidity is excessive or nil. Disturbances of the normal distribution of acidity in general seem to be inimical to digestion. While the alizarin test may not be reliable for the estimation of combined hydrochloric acidity, any great difference between the readings of acidity by dimethylamidoazobenzol and alizarin indicates fermentation acidity, and if the sum of free hydrochloric and so-called combined hydrochloric acidity does not nearly equal the total, the peptonization is usually low. For instance:

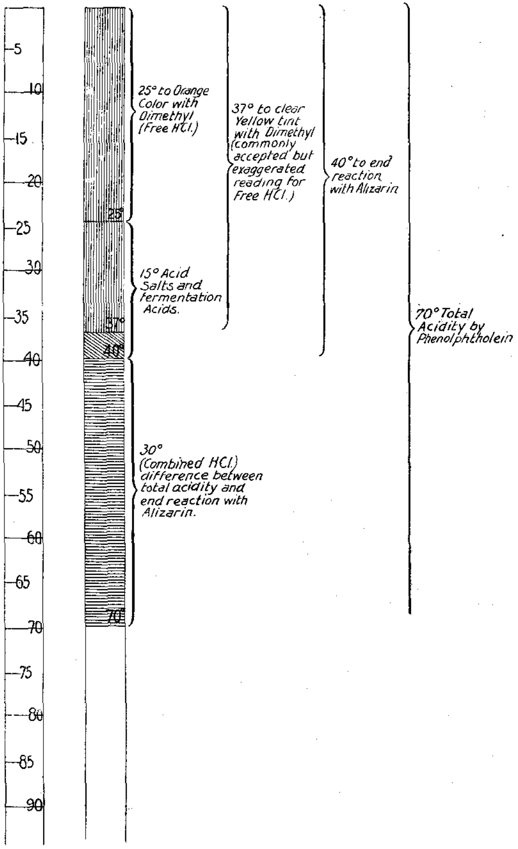
	Total.	Free HCl.	Combined HCl.	Fermentation.	Albumin.	Albumose.	Peptone.
F. G	85	15	27	85—(15+27)=43	1	trace.	10
J. B. B.	78	8	53	17	4	¼	22
G. L. S.	77	10	50	17	5	trace.	31
M.	80	34	37	9	2	......	23
E. A. S.	78	28	33	7	trace.	......	22
W. J. B.	70	22	23	25	½	......	14
J. P.	89	41	25	23	4	¾	17
C.	74	10	42	22	4½	1	16½

We cannot expect a very close correspondence in such examples, although I have selected several in which the total acidity is about equal. The phenolphthalein test for total acidity is fairly sharp and accurate. The alizarin reaction is sharp, but probably not very accurate. The dimethylamidoazobenzol test for free HCl is neither. As reported in the series of notes published in *American Medicine*, 1902–1903, the tedious method of titrating without an indicator and removing a drop of the investigandum from time to time and testing it with resorcin and sugar, has convinced me that an exaggerated reading for HCl is obtained, if we note the final but sharp end reaction with dimethyl. Instead, we must take the reading when the first slight but distinct change occurs from cherry to orange. This change occurs about fifteen degrees before the end reaction occurs, but I am unable to decide the point of change within an error of five degrees. As the alizarin method of estimating combined hydrochloric acidity is merely one of subtraction, it is immaterial for our present purposes whether this test is reliable or not, but the fact remains that when there is a considerable acid factor between the dimethyl reading and that by alizarin we may anticipate a low peptonization. This point may be illustrated by the diagram on opposite page. Unfortunately, we do not understand exactly how the acid salts and fermentation acids affect the various indicators. Apparently, a free organic acid acts precisely like a mineral acid, but much less energetically, and although I am convinced that the common practice of reading free hydrochloric acidity at the end reaction with dimethyl gives an exaggerated value and leads to the diagnosis of hyperchlorhydria in many instances in which there is really euchlorhydria—perhaps temporary—we must remember that all titration methods are purely approximate.

The method of proteolysis described, though approximately quantitative, must be thought of—like the acid estimations—as the measure of a rate of progress instead of a distance covered. There is no way of measuring the absolute amount of material digested by or in the stomach. We can, of course, weigh and analyze the entire test meal before ingestion and an hour or so afterward, resorting to thorough lavage. But we cannot be sure that some portion of the meal has not passed the pylorus undigested; on the contrary, we can be reasonably certain that considerable loss has occurred in this way.

The method described is more simple and easy and, *a priori*, more logical than those based on measuring the "left-over" digestive power. That it is crude and contains fallacies, is obvious, but all methods applied clinically to the very meagre amount of investigandum obtainable are subject to this limitation. I am rather prejudiced in favor of the use of centrifugal volumetric estimations for various clinical purposes, believing them to be more accurate on the whole than gravimetric methods employed under the unfavorable conditions common to most clinical investigations and than most clinical adaptations of elaborate methods, such as the Kjehlaahl nitrogen determinations. Meanwhile, assistance is desired in noting fallacies and in discovering more accurate means of separating the various proteids.

TYPIC TITRATION OF CHYME.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70°
25° to Orange Color with Dimethyl (Free HCl.)
37° to clear Yellow tint with Dimethyl (commonly accepted but exaggerated reading for Free HCl.)
40° to end reaction with Alizarin
70° Total Acidity by Phenolphtholein
15° Acid Salts and fermentation Acids.
30° (Combined HCl.) difference between total acidity and end reaction with Alizarin.